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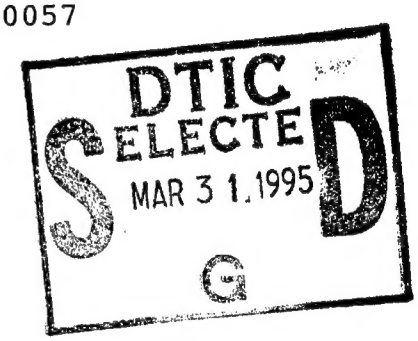

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Fort Detrick
Frederick, Maryland 21702-5012

December 19, 1994 Annual (1 Dec 92 - 20 Dec 93)

Coordinated Approach to Breast Cancer Diagnosis and Treatment for the Military (Core Program)

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The Georgetown radiology research team has five separate but related grants on digital mammography. This core administrative grant provides support functions to four related interactive grants. This report is for the core administrative grant and it summarizes four related projects.
A new Computed Radiography (CR) with new high resolution plates are under evaluation and the initial results are positive. We expect to start a full scale clinical trial during the second year. A new 42/21 micron film scanner has been tested favorably at DBA factory and the scanner will be delivered to Georgetown during the spring of 1994. A new digital mammography system based on amorphous selenium detetcor of 3M is under construction and prototype system is expected at Georgetown during the spring of 1994. Initial testing at the factory is very encouraging. Telemammography and MDIS compatibility is being studied in collaboration with Siemens Gammasonics, software developer of MDIS project. Mini database of MDIS has been installed at Georgetown and interface is under development. Computer aided diagnosis is now looking at second order effect. We are focusing on characterization of microcalicifications, detection of masses and possible approach for insertion of CADx in clinical decision making process. In summary we believe that digital mammography will be possible and may prove to be better than conventional mammography within the next several years.

Breast Cancer, Diagnosis, Military, Treatment

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Coordinated Approach to Digital Mammography

Report on the First Year of Project

1.0 Introduction

There are three components required for the successful development of a digital mammography system: image data acquisition, image processing, and image display. The Georgetown radiology research team has five separate but related grants on digital mammography to address technical issues in a coordinated manner. One of the five grants deals with administrative support functions to four related interactive grants on digital mammography. Detailed individual reports have been submitted to the Army. This report will summarize all four related projects in a concise format. Readers are encouraged to refer to the individual reports for the detailed information.

2.0 Summary of Tasks

Extending Current Technologies of Computed Radiography (CR) and High Resolution Film Scanner

Mammography Based on Amorphous Selenium Detector of 3M

Telemammography and MDIS Compatibility

Computer Aided Diagnosis

3.0 Coordinated Project Summaries

3.1 Extending current technologies

3.1.1 Digital mammography

There are two methods of creating a digital mammogram: direct digital acquisition and digital transformation of an analog image. Direct digital mammography systems, existing or under development, use storage phosphor plates, charged coupled devices (CCD), selenium plates or electron capture devices. Film digitization devices can be based on laser, monochromatic or diffuse light.

Direct digital mammography devices: A survey of existing direct digital mammography machines revealed that only Fuji Corporation had a working FDA approved system for digital mammography. We acquired such a system for testing in September 1993. No other existing commercial machine was identified. Research devices are under development by Dr. Martin Yaffee in Toronto, by Lorad Corporation, 3M, and by Fischer Corporation in the U.S. and Fuji Corporation in Japan. In addition, several smaller companies such as Photometrics and Princeton Instruments are exploring various devices. We are working with 3M and with Princeton Instruments on their machines and have had discussions with Photometrics, Lorad and others. These devices are not yet finished and were unavailable for testing. Images from some of these machines have been reviewed. Currently the Lorad images are the most promising, but we were unable to do a true assessment of the machine.

Film digitization for digital mammography: There are existing devices for film digitization based on laser or CCD technology using 100 to 200 micron pixel sizes available from multiple vendors including Lumisys, Vidor, Vision 10, and others. There are a few companies claiming 50 micron digitization capabilities, usually over a limited range of optical densities. We have been investigating the technology under development by DBA, Inc. This 42 micron pixel system will be delivered to us in March 1994. Evaluation studies are in progress. Should film digitization prove to be an appropriate technology for further investigation, then the required pixel size for this technology could be determined. Tests to determine the preferred contrast characteristics for

mammograms to be digitized will be performed.

3.1.2 Resolution requirements for digital mammography

Publications on digital mammography implied that the development of a digital mammography system would require the development of new detectors because existing systems did not have adequate resolution. There are a few articles describing that 100 micron pixel size appears not to be sufficient. It was suggested that resolution of digital mammography should be equal to the high contrast resolution of screen-film mammography — 20 line pairs per millimeter (lp/mm).

Oestmann reported that while a 5 lp/mm storage phosphor system was sufficient to detect all clusters of microcalcifications, that individual microcalcifications were less visible at this resolution. He reports that he selected image processing settings that resulted in images "similar to those we obtained of conventional mammography." He used the same exposure as that used for the conventional screen film images he obtained for comparison (30KVP at 250 mAs). This is a higher KVP than would normally be used for conventional mammography and would be expected to decrease the contrast of calcifications on the conventional images (our most common setting is 26 KVP).

Chan, reporting on the use of high quality film digitization at 100 micron pixel size, found that digitized mammograms provided lower detectability of subtle microcalcifications than conventional screen film mammography. She found that unsharp masking improved the detectability of the calcifications, but even with unsharp masking, the conventional screen film mammograms still had a higher detectability rate.

The two articles mentioned above (Oestmann and Chan) suggested that 100 micron pixel size was insufficient. Screen-film mammography systems can have up to 20 lp/mm of high contrast resolution. This would imply that one would need a system with 25 micron pixel size to equal the high contrast resolution of screen-film. The only contemplated systems that we are aware of that come close to this resolution are film scanners. If indeed this resolution was required, then all of the direct digital systems under development would end up being insufficient for digital mammography. Because of this we undertook both an experimental and theoretical approach to determine the effect of different pixel sizes on the detection of very small radiodense objects. The theory will be presented first followed by the experimental evidence that supports it. This will then be followed by a discussion of the implications of these findings for further research.

Theoretical model of pixel size requirement: In this model we have assumed that the shadow from the calcium fleck will be maximally offset from the center of the pixel. In actual practice one would expect that intermittently, the shadow would fall directly on the center of a pixel and thus one could occasionally see a calcium object that is the size of the pixel (assuming that the calcium object and its penumbra completely fill the pixel. Calcium flecks intermediate in size between pixel size and $2A\sqrt{2}$ have an increasing chance of having their shadow projected directly over a pixel with the likelihood increasing as the size of the calcium fleck increases. The formula $2A\sqrt{2}$ is the size necessary to assure visualization.

In actual experiments, one does slightly better than this because the focal spot size in finite and therefore there is a penumbra around the small object enlarging its projected size. Thus, in tests, we can just faintly see the 160 micron object with 83 micron pixel. While this suggests that one may need only 2A, rather than $2A\sqrt{2}$ to see an object with contrast enhancement using image processing, actual measurements of the objects in the phantom indicate that as projected onto conventional screen film systems, that the objects and their penumbra are actually larger.

Measured size of calcifications in breast biopsy specimens: Measurements using an 8

X magnifier and measuring reticle demonstrated that in 10 contact specimen biopsy radiographs (20 line pair system) most of the calcifications that could be resolved as individual objects measured 300-600 microns. There were some 200 micron calcifications that could be individually identified, and then there were areas of calcification with particles that could not be resolved. Since this tested system has less noise, less scatter, and less penumbra than any conventional screen film mammogram could have, we believe that the lower limit of size that we need to resolve for clinical purposes in 200 microns.

The clinical applicability of this is that when there are malignancy associated calcifications, there are often many of them and they may be superimposed on each other, and thus visible at a smaller size. While this will help in many cancers, there are cancers with only a few calcifications. These will not have superimposed calcifications and will not demonstrate this phenomenon.

Work done in our labs indicated that film digitization at 170 microns was insufficient to allow detection of smaller microcalcifications. We have done a limited amount of investigation of an experimental 35 micron film digitizer at the manufacturer's facilities. The preliminary studies suggest that the use of a 35 micron film digitizer coupled with appropriate image processing may allow the replacement of direct geometric magnification with electronic magnification. With electronic magnification, the conventional screen film image is digitized at 35 microns. A small section of this is then displayed as an enlarged image. With appropriate image processing, it is possible to see calcifications and details in shapes of calcifications that cannot be seen either directly or with a magnifying glass on the original image.

The benefit does not appear to come from the magnification, since the type of hand held magnifier commonly used by radiologists when they interpret screen film mammograms is sufficient to detect 30+ line pairs per mm of high contrast detail. The benefit appears to result from the image processing that allows improvements in object contrast that occur from gray scale changes and edge enhancement. Our experiments suggest that film digitization with very small pixel sizes may prove to be a viable method for digital mammography.

3.1.3 Decreasing exposure using digital systems

In our tests, we found that the Fuji high resolution plates appeared to require the same exposure as our standard screen-film system for the demonstration of equal information. In the experiment comparing the effect of decreased exposure on detectability of objects in the CDMAM phantom, we found that at the lowest exposure level tested that the digital system performed better than the screen-film system. However, we found in a small sample that only 1 of 20 of our cases had any region in the breast with such a low exposure and that these regions were clinically underexposed. Once this minimal exposure is exceeded, the screen film system performed better. This was an early experiment before we had reached our current knowledge of image processing, and will need to be reevaluated. Our preliminary data suggests however that there will be no potential decrease in exposure possible, unless one is willing to work with less information than screen film systems provide.

Other work in which we did direct geometric magnification onto a standard phosphor plate demonstrated that with appropriate image processing, one could see more on magnification views with a low exposure than on magnification views recorded on screen film systems. This result suggests that one should evaluate the value of doing geometric magnification views at a higher sensitivity, but lower resolution, film than is currently used for standard mammography. Other work done elsewhere suggests that there may be value in using direct geometric magnification on all mammograms.

3.1.4 Image processing

Image processing is the second major component of digital mammography. Correct image processing enhances the visibility of abnormalities in digital images. Incorrect image processing can conceal information. There have been a few publications on optimizing image processing in chest images including several of our own, but we are not aware of publications on optimizing image processing in digital mammography. We presented our preliminary material at the annual meeting of the Radiologic Society of North America in December 1993 (13) and at the meeting of the Society of Photo-optical Instrumentation Engineers (SPIE) in February 1994. This report will be published as part of the SPIE Proceedings. Apart from our own work in image processing in digital mammography and limited work done by Chan on digitized film images, we are unaware of any similar work.

Image processing as currently available consists of three main potential changes in the image. These are changes in the look-up table (LUT) to affect optical density and contrast, changes in spatial frequency to effect either edge enhancement or noise reduction, and methods for balancing the optical density in an image (often called histogram equalization) in order to better match the original information to the characteristics of the display device used. Each of these provides an important advantage to diagnose breast cancer on digital mammography. Image processing can be used on any digital mammographic image, independent of the method used for acquiring the digital image. The techniques are the same for different digital detectors and for both direct digital and film digitization methods.

Changes in look up table: Look up table maps exposure level received by an imaging plate to a specific optical density or luminance on the display device. This mapping is important because the original receptor may be linear or nonlinear in its response and all current display devices are nonlinear, with different response characteristics. If one considers only the display devices, for the moment, the response characteristics are characterized by a nonlinear S-shaped curve. This curve, described for screen-film system as the H & D or characteristic curve, is also reflected in the pattern of display seen in the luminance values on monitors.

The characteristic curve is S-shaped and is usually divided into three sections for discussion purposes: The toe, the shoulder and the central portion. The contrast in the toe (bottom) and shoulder (top) of the curve is less than that in the central portion of the curve. For digital mammography, the most important regions are the toe (the region of low exposure) and the central portion (where the highest contrast is). The dense breast is one in which there is a large amount of tissue that is close to the density of calcium. If this region of breast density is mapped into the toe region of the characteristic curve, then calcifications will be more difficult to see. If the calcifications are projected in a region of increased breast radiodensity, then they will be of low contrast compared to the background tissue and therefore more difficult to see. The application of changes in the LUT to change the final optical density and contrast are to change the optical density of the region where calcium could be partially obscured by shifting densities to the region above the toe of the characteristic curve and to increase the slope of the characteristic curve in regions of increased breast radiodensity.

In our evaluation of changes in the LUT, we recorded the characteristic curve of the screen film system currently used for mammography, a second screen film system, and then measured the optical density of mammograms in our collection at the sites where cancer had been found. In 1 of the 20 measured, the microcalcifications associated with the cancer were in a region where the optical density of the region of that breast was in the low contrast region of the toe of the characteristic curve. Thus a simple remapping of the optical density to a region above the toe of the characteristic curve would have improved the detectability of the calcifications in 5% of this small sample. A second experiment in which we changed the LUT of a digital image of the CDMAM phantom so that it was printed at different optical densities confirmed that there was a lower

detectability of objects at a low OD. However, once it was above the toe of the characteristic curve, the detection rate did not change over a wide range of OD values.

Increasing the contrast in the steepest portion of the characteristic curve should also help in the detection of microcalcifications. Our preliminary tests suggest that there is a limited effect from a contrast value of roughly GA = 0.8 to GA = 2.5. Above and below this range, the detectability decreased. Within this range our preliminary results showed no change. Above GA = 2.5, the accentuation of noise limited the visibility of objects in the image of the phantom.

Spatial frequency changes: All images are composed of a combination of many spatial frequencies. High spatial frequencies correspond to sharp edges. Low spatial frequencies correspond to smooth edges. Several methods exist for altering the spatial frequency patterns within an image. Our work was done with a method called unsharp masking using a convolution kernel of various sizes. In this method, a kernel representing an array of numbers is multiplied by the pixel values in the image changing its final appearance. In the Fuji method used, kernels of different sizes are named as settings of an RN factor and vary from 0 to 9. The emphasis given to this spatial frequency effect is named the RE factor and varies from 0 to 16. In addition there is an additional effect acting on the image only in regions of low optical density called the RT factor. The RT factor is used to decrease the visibility of noise at low exposure/low optical density regions of the image.

We tested various combinations of RN, RT, and RE settings in mammography phantoms. Our results indicate that the detection of microcalcifications is improved by small kernel sizes and by intermediate to high settings of frequency enhancement. Larger kernel sizes helped in the detection of small masses. None of the factors tested had much effect on the detection of fibers. Because the best detection of microcalcifications occurred with the smallest kernel size, it is possible that a still smaller kernel size could offer additional improvement. We found that certain settings, especially those with a larger kernel size or with a large amount of spatial frequency emphasis, improved the detectability of objects in mammographic phantoms, but resulted in unusual appearance of image that may cause radiologists to reject the images. A setting that best demonstrated small masses could also obscure microcalcifications. Based on our preliminary data we now consider that settings GA = 1.5, RN = 9, RE = 5 to be a partially optimized set of values for image processing of digital mammography.

Optical density adjustment methods: The range of radiodensities in the breast is wide and their distribution is unequal. On conventional screen film mammography it is difficult to have adequate contrast in the more radiodense regions of the breast and still have sufficient range of visible densities to adequately see the skin thickness. There are available methods for adjusting the range of optical densities within a final image that allow different optical density regions to have different LUT. These methods, sometimes called histogram equalization methods, could be useful in the display of digital mammography. In late December 1993, we had such an investigational device implemented on the Fuji system used for digital mammography. We will be investigating the effect of this in 1994.

3.2 Mammography based on amorphous selenium detector

3.2.1 High resolution detector based on selinium detector

One approach to a digital x-ray detector is to use a photo-conductor that generates hole-electron pairs in response to the x-ray flux, which are separated by an electric field and stored as a latent image for later readout. A prototype digital x-ray imaging system under development by 3M consists of an x-ray detector and an image reader. The x-ray detector is a thick-layer amorphous selenimum and insulation layer device that stores the x-ray latent image as a charge distribution at the selenium/insulator interface. It can be modeled as two capacitors in series, with charge injected

through the photoconductor of the pc-isolator interface by radiation. The reader is a scanning device that uses a pulsed HeCd laser (441 nm) to read the latent x-ray image stored in the detector. The image reading laser pulse releases the latent image charge from the interface. The released charge is detected, digitized, and stored by the image reader.

The prototype device operates with a large dynamic range and produces linear x-ray signal response for clinically reasonable x-ray exposure. Clinical quality images can be obtained at x-ray exposures that are comparable to those used for state of the art film screen systems. The resolution of the image (pixel size and pixel spacing) is determined by the size and placement of the image reading laser. The prototype is routinely operated at resolutions from 50 micron to 170 micron.

The performance of the device compares well with theoretical results. A wide dynamic range Initial results show linear x-ray signal response to x-ray dose for low exposures, and a large dynamic range. For example, with typical parameters (430 micron Se, 188 micron insulator, 10 volt/micron field) the model x-ray-signal from the readout use 0.35 nC/sq.cm per mR, with dynamic range to 30 nC/sq. cm at 200 mR x-ray exposure.

Currently, final engineering work is underway for the prototype system to be shipped to Georgetown for clinical installation. It should be noted that the development of the system is entirely funded by 3M and it is outside the scope of this project. Technical collaboration and clinical evaluation are part of this funded project.

3.3 Telemammography

The research from the first year has demonstrated the requirements for image acquisition and has demonstrated appropriate parameters for portions of the necessary image processing. This project deals with investigations related to image display, which are at a preliminary planning stage, but some of the necessary criteria have been already defined.

3.3.1 Image display

Image display is an essential part of digital mammography. Conventional screen film mammography allows the display of 20 lp/mm of high contrast information. At the lower contrast range in which mammography falls, however, there is only somewhere between 2.5 to 5 lp/mm actual resolution. Conventional breast images are most often 8 x 10 inches, but in about 10% of cases, 10 x 12 images are produced.

There are two potential methods for the display of digital mammography: Display on workstations and display on laser prints. These two methods for display of digital mammograms are limited in their capabilities and new methods are unlikely to emerge in the near future.

When one displays digital information, the display can be of different sizes. One therefore has to consider the number of pixels in the total display as well as their spacing. Using a larger monitor does not increase the number of pixels displayed, but may display them at a size that is easier to interpret due to the magnification resulting from the larger display. With laser camera prints, the limit is 300 dots per inch. The larger the film, the more pixels that can theoretically be displayed.

3.3.2 Pixel size and related factors

Display on a workstation: The highest pixel number available on workstation monitors is 2048 x 2500 pixels. If one is projecting an image of the breast originally obtained on an 8 x 10 inch receptor, this implies that one would be limited to displaying 100 micron data if one wished to display the entire image at one time. As indicated above, this would result in an image that would approximately equal the image of screen film mammography.

If one captured the data at a smaller pixel size, one could not display the entire image at this higher pixel size, but would have to scan through the image region by region magnifying each section of the image to assure that no microcalcifications were present.

Display on a laser print: Laser printing systems are currently limited to a resolution of 300 dots per inch (DPI) which converts to about 86 microns per pixel. Films of size 14 x 17 inches are then equivalent to a matrix of approximately 4000 x 5000 pixels. Thus an 8 x 10 inch image digitized at 50 microns per pixel will be displayed at a size of 14 x 17 inches. If one chooses to display the image close to its original size of 8 x 10 inches, the original image will need to be digitized at a resolution close to 86 microns per pixel.

The effect of image display size on a workstation monitor: Workstation monitors are limited to approximately 2000 x 2500 pixels. As one changes the size of the monitor, the number of pixels remains the same, but the size of each pixel in the display changes. When radiologists interpret screen film mammography, they usually use a magnifying lens to magnify the microcalcifications to make them more apparent. Typical magnification glasses used are 2 X or 3 X magnifiers. Based on our tests, the use of such a magnifier allows as much as 30 line pairs of high contrast detail. Thus this use of a magnifier lens exceeds the high contrast resolution of screen film mammography. The best display size for digital mammograms is yet to be determined. Based on the measurements made with the hand magnifier, in 1994 we will test monitors of different sizes using monitor displays of different sizes and image processing optimized images of breast phantoms. Our hypothesis is that displaying the image at 1.5 X normal size (12 x 15 inches) will likely provide full benefit, but we will also test larger sized monitors.

The effect of image display size of laser prints: Current laser printing technology is limited to 300 dots per inch. The laser printing technology discussed here is with regard to printing on a transparent film with 10 bit gray scale to produce images that can have optical density greater than 3.0. It is important to note that printing on film to produce optical density greater than 3.0 with about 10 bit gray scale is different from printing on paper in reflective mode. Paper laser printers can offer resolution much higher than 300 DPI. However, laser film printers, available in the market of medical imaging, can only have a resolution of 300 DPI or less. According to our industrial sources, higher resolution systems are not likely to be developed in the near future. There are at least two different methods of positioning information within each of the dots: the standard half-tone method and the Scitex patented method which divides each dot into multiple smaller dots for printing purposes (15). The Scitex method currently only prints on paper, but appears to give a visually smoother image than halftone methods, meaning that the edges of pixels are less apparent on image magnification. We are working with Scitex to test their system for the display of digital mammography.

3.3.3 Look-up table factors

Laser print film and workstations have different characteristic curves than conventional screen film mammography systems. Tests would have to be performed to optimize the display of digital mammography for each potential system. Laser printers and films differ in their response characteristics and different monitors differ in their response characteristics. Procedures for measuring differences between laser systems and monitors need to be analyzed so that the optimization procedures could be applied across different manufacturers' systems. We and others have done some preliminary work on monitor displays (14) and this will be an essential aspect of our work in the next two years of the project.

3.3.4 Mammography workstation performance features

The following MDIS compatible workstation performance features are the result of collaboration with Major Donald Smith, M.D., Clinical Coordinator of MDIS at the Madigan Army Medical

Center.

Display monitors: The mammography workstation will have four 2.0 k x 2.5 monitors. The monitors will be arranged in an adjustable amphitheater-like setting. The monitors will be used in a portrait mode. The workstation shall accommodate individual images with a 4k x 5x by 16 bit deep images (40 Mbyte of data/image).

Brightness (Luminance): The brighter the monitor the better, as long as spot size is not compromised. The goal should be to have a monitor greater than 100 foot-lamberts.

Gray scale display: No fewer than 256 shades of gray (8 bits deep) displayed on each monitor shall be provided.

Refresh rate: The monitor is to be flicker free for 95% of observers with a SMPTE pattern displayed when adjusted to 90% of maximum intensity and observed under maximum ambient illumination of not greater than 10% of the monitor intensity. This should be greater than 70 Hz.

Noise: The monitors shall not have any observable electronic noise.

Calibration: Brightness and contrast adjustment range of the monitors shall support matching of the monitor gray scale displays to < 5%. Three-month drift of monitor brightness and contrast shall be < 5%.

Uniformity and distortion: The monitor shall have less than 15% brightness uniformity degradation from the center to the periphery. The monitor shall also have less than 3% linearity and 3% geometric distortion from center to periphery.

Monitor electron beam spot size: The spot size shall vary less than 50% from center to diagonal corner of each monitor. This is measured from a viewable area 1/2" inside the perimeter of the monitor.

Frame buffer: The frame buffer should be no less than 16 bits deep. This is to accommodate 16 bit film digitizers now in prototype stages.

Random access memory: The RAM memory shall be capable of holding at least the full data set of four mammography images. Any additional images required from local storage will be accessed in a manner seamless and transparent to the user.

Local storage: When used in a stand alone mode, the workstation will have enough memory to accomplish one day's worth of work. One strategy would be to store the exam in a compressed format on the magnetic media and decompress the data on the fly to the video frame buffer in order to reduce the local storage requirements assuming that the compression used does not significantly compromise diagnostic image quality. Each image without compression represents 4k x 6k by 12 bits deep, as is considered in one prototype unit.

Image display speed: The display speed of an image from local storage must be 2 seconds or faster. Re-display of an image from RAM will be 1 second or faster.

Image acquisition input: The directly digital mammography images will first be viewed at a one or two monitor quality control workstation. This workstation will have similar functionality as the diagnostic workstation with multiformat image capability. It might need a 2k monitor also in order for the technologist to see if magnification or repeat images have the area(s) of subtle microcalcifications that the radiologist has requested for additional view.

Archive connectivity: Images of previous exams and associated reports will be loaded to the local storage of a workstation automatically from a high capacity optical archive (e.g. optical jukebox) based on scheduled exams list. Alternatively, the associated reports might reside in local storage and automatically be displayed with the exam on demand. The ultimate goal is to interface to the MDIS system.

3.3.5 Workstation functions

The workstation shall provide multiple image manipulation and enhancement functions through use of a graphical user interface (GUI). The selection of these functions will be done by pull down menus, soft buttons, and quick key options. The pull down menus and soft buttons must be duplicated on each monitor. The following are required performance parameters.

Work/Patient List
Soft Buttons
Image Selection
Image Rearrangement and Display
Multiformat Image Tool
Double Click Image to Full Size
Default Display Protocol
Next Exam
Image Enhancements Defaults
Edge Enhancement
Window and Level
Inverse Video
Cursor
Screen Blanking
Automatic Shutdown
Zoom
Image Roam
Digital Magnifying Glass
Rotation and Flip
Mensuration
Text and Graphics Annotations
Identification
Delete
Hard Copy Generation
Command Reversal (Undo)
Save
System is Working (SIW)
Reporting

The workstation will allow the use of the ACR reporting software, Breast Imaging Reporting Database (BIRD) program. This program provides the standard lexicon of terms used in mammography reports. This approach may require an additional standard VGA monitor and CPU integrated as far as data sharing with the diagnostic workstation but usable with a separate or same mouse as two options. The separate mouse would be used when a staff radiologist is working with a resident and one could be using the diagnostic workstation and the other is inputting the report. A single mouse would be used when only one person was working. A laser printer will be connectable to the workstation for hard copy report generation. The analysis of the database information will be possible using Microsoft Excel or similar spread sheet programs. This tool will be chosen by pull down menu or quick key options.

3.3.6 Follow-up exams

The exams that require an additional view when the patients are called back must be tracked in an effective and transparent way to the technologist and radiologists. A utility to confirm the requested follow-up exams is mandatory. A method to place the exam back on a specific radiologist's work list is necessary. An option to log in scheduled absences of the radiologist is needed so that any call back patients will have their exams interpreted without delay by the reader for that day. This way the routinely assigned mammographer for the day will read the call-back exam. The list of call-back patients will include the patient demographic data, especially the patient's phone number.

3.3.7 Additional image marking

A moveable region of interest for focal cone compression, focal cone magnification compression or simple magnification at 1.5 magnification (or other designated magnification factor) will be identified within a fixed field of view for a given image. This image shall be stored as an overlay to the original image. This information will be sent back to the QC workstation to be matched up with the patient's image for the technologist's reference in order to accomplish the additional view(s). The images obtained as focal cone compression, focal cone magnified or simple magnification views will be marked as such on the image along with the degree of magnification. The ROI will be moved to the area of concern by using the mouse and deposited with a mouse click. These choices will be indicated by pull down menu, quick key, or soft buttons.

3.3.8 Surgical and core biopsy results input

A method to quickly input the pathology results from surgery and core biopsies into the patient database will be provided. Ideally, this input can be input to the QC workstation and then downloaded to the mammographic diagnostic workstation by using standard site configurable language. The selections will be mouse driven with input of nonstandard language by keyboard. Scheduling of patient biopsies will be part of the results reporting utility.

3.3.9 Computer assisted diagnosis (CADx)

The workstation must have hardware capability for CADx. The image processing must occur automatically in the background and not interfere with interactive image manipulation for the displayed exam. The CADx for a four image exam must take less than 30 seconds. At least three different levels of sensitivity must be user selectable. The displayed areas of interest identifying masses and microcalcifications will be marked with variable size graphics (e.g., circles or arrowheads) that can be toggled on and off. The variable size of the markers as an overlay will indicate the position and degree of confidence of the finding being a true positive. When the user is ready for display of this overlay a pull down menu, quick key, or soft button will be used. The CADx software should also allow for a pointing function to allow the user to select an ROI and query the CADx program for its analysis of that location.

3.4 Computer aided diagnosis

Many investigators have attempted to analyze mammographic abnormalities. Recently, several investigators have proposed various methods for the automatic detection of microcalcifications and masses on mammograms. The accuracy of the computer algorithms for the detection of microcalcifications have been further improved since the initial attempt by Chan et al. We believe that it is important to implement the program in a high speed workstation and conduct a large scale pre-clinical trial in order to evaluate its clinical practicability and limitations. It is known that the false-positive rate is still very high for the detection of masses. We believe that a more useful and fundamental approach to computer-aided diagnosis is to devise a computer program to analyze

features of suspected masses. We propose to use an artificial neural network to classify malignant and benign masses.

Because of the need for high resolution of digital mammography, data compression is an important means to facilitate the mammographic image transmission and storage. We have studied some characteristics of the mammograms using gray value splitting and full-frame DCT methods. Effects of the data compression on the CADx in the detection of the microcalcifications were also tested in our preliminary evaluation.

3.4.1 Image processing prior to the detection of microcalcifications

At Georgetown, a band-passed filter was newly developed based on a wavelet transform. Since the wavelet transform can decompose both frequency and local spatial information into its transform domain, some breast tissue structures (e.g.; vessels and ducts) can be easily extracted in the transform domain.

In the wavelet transform, many line structures were extracted to three different high frequency regions: horizontal, vertical, and diagonal. In these regions, one can easily detect the line and band structures using modified Hough Transform. Removed lines and bands are compensated by a relaxation algorithm in the original image. Once these background structures are reduced, the microcalcifications can be more accurately extracted in the following CADx detection procedure.

3.4.2 CADx algorithm in the detection of microcalcifications

We also have made great effort in the improvement of the original CADx program. The microcalcification searching algorithm, which was a bottle neck, has been greatly improved. The new program uses "the chain algorithm" to search for the boundary of each island based on a given threshold. The suspected microcalcifications, which are "islands" in a large image, are tested by histogram thresholding method and root-mean-square variation method.

We have started to implement the CADx program on a DEC Alpha workstation, which currently is the fastest workstation in the market. The basic user interface is nearly complete; however, it requires some final polish. The user interface can select a mammogram and display on the workstation. Several basic image functions are also available: (1) "window and level" for the adjustment of the brightness and contract, (2) pan, and (3) a cursor box for the user to select the area of interest.

3.4.3 CADx algorithm for classification of microcalcifications

A computer vision scheme that can classify microcalcifications in digitized mammograms were developed to help radiologists in the diagnosis of breast cancer. The radiographs of pathological specimen of microcalcifications were digitized using a small pixel size of 21x21 μm. Regions of interest (ROI) that contained clustered microcalcifications were selected and used as input to a convolution neural network (CNN). The diagnostic performance of the CNN was evaluated by ROC analysis, using the area under the ROC curve (A_Z) as a performance index. The CNN achieved an average A_Z value of 0.90 for classifying microcalcifications associated with benign and malignant processes. Classification of microcalcifications associated with benign and malignant processes is feasible with the high resolution digitization of mammograms. The convolution neural network appears to be an effective tool in the classification task.

3.4.4 Mammographic image compression

Based on the splitting method which was employed to reduce edge effects and to obtain maximum

compression efficiency, we have refined our compression method using alternate value contour coding and full-frame entropy encoding. We have tested 15 digitized mammograms, formatted 2048 x 2500 x 12 bits.

Error-free compression for images containing most significant values: We have developed an efficient compression method called "alternate value contour coding" for the step-type image. The most significant value images containing the 3 most significant bit (3MSB) of digital radiographs belong to this type of image. We have tested the newly developed compression method on chest radiographs. This method performed much better for error-free compression than DPCM/run-zero/arithmetic coding proposed earlier due to the method of turning the entire 2-D image data into a l-D edge tracking sequence. In addition, contouring for the adjacent values is ignored and the image data is fully recoverable The only drawback of the alternate value contour coding is that the algorithm is somewhat complicated and demands error checking procedures to ensure the error-free requirement is fulfilled.

Compression for images containing least significant value: Based on the full-frame entropy encoding (FFEC), the remapped 9 least significant value (R9LSB) images were decomposed by 2-D full-frame DCT followed by a quantization procedure and an entropy coding (arithmetic encoding) as indicated in our proposal. Preliminary results obtained from the studies using the proposed methods are listed as following.

We have evaluated the density distribution of DCT coefficients for several chest R9LSV images. We found that the distribution density of R9LSV image fits in a Gaussian model. However, the standard deviation of the Gaussian distribution tends to be large, which makes the nonlinear quantization [Max 1960, Modestino 1985] less useful. The reason for a broad Gaussian distribution is that the low bit data contains a much lower signal to noise ratio. It is relatively difficult to quantize and to encode noise dominated images both in the spatial and in the frequency domain. Our initial results indicated that the advantage of using a nonlinear quantizer over a linear quantizer is very small (about 5-8%) for R9LSV images.

As far as RLSV images are concerned, the FFEC is the primary algorithm. We found that digitized radiographs containing not only white noise but also system structure noises (e.g., system electronic and mechanical noises and dust on the computed radiographic plate or lens). Although the proposed splitting method has partially solved problems related to sharp edge effects, spots and shallow lines are the main structures for encoding. We therefore spent some time overseeing image quality and consulting with vendors to adjust our computed radiographic and laser film digitizer systems. However, we did not succeed in overcoming all the structure noises, particular in film digitizers. We have evaluated images with a step wedge and found that a minimum of 4 of the least significant bits out of 12-bit values are noise. These results are confirmed by both signal to noise (S/N) and covariance studies with single displacement. Among the sampled gray spectrum, the maximum S/N is 120. By taking up to 4 least significant bit data through round-off, the maximum covariance is less than 0.07. However, the test of covariance is drastically increased to 0.2 with the 5 least significant bit data. These results indicated that the image data contained only about 8 bit information. Based on these noise characteristics, we can limit our frequency quantization corresponding to gray value variance.

Effects of image compression on detection of microcalcifications: Our previous ROC study indicated that detection accuracy of microcalcifications by radiologists is significantly reduced if mammograms are digitized at 0.1mm. Our recent study also showed that detection accuracy by computer decreases as the pixel size increases from 0.035mm. It is evident that very large matrix sizes have to be used for digitizing mammograms. Efficient compression techniques will be needed to facilitate communication and archiving of digital mammograms.

In this study, mammograms were digitized with a laser scanner at a pixel size of 0.035mm and 12

bits. We studied two compression techniques: (a) full frame discrete cosine transform (DCT) coding with entropy coding and splitting of bits, and (b) Laplacian pyramid hierarchical coding (LPHC) with linear requantization. The effectiveness of the techniques is compared in terms of the bit rate, the mean-square-error, the visual quality of the reconstructed and error images, and the detection of microcalcifications by computer.

With LPHC, significant degradation of detection accuracy was observed when the compression ratio was greater than 3.6:1. The DCT technique provided higher compression efficiency at comparable detection accuracy. A compression ratio of 9.6:1 was achieved without significant degradation in detection of microcalcifications. Furthermore, it was found that the mean-square error was not a good indicator for evaluation of information loss due to image compression.

In conclusion, our study showed that there is a trade-off between reconstructed image quality and compression efficiency. Further investigation is needed for selection of optimal compression technique for digital mammography.

4.0 Activities for Year 2

4.1 Extending Current Technologies

Two technologies under study are high resolution film digitizer and computed radiography. A new film digitizer manufactured by DBA Inc. will be studied at 42 micron and 21 micron focal spot sizes. Evaluation will have clinical and technical components. A computed radiography system, Fuji CR 9000, will be tested with new high resolution plates and new image processing software. The amount of radiation exposure will be studied.

4.2 New imaging system from 3M

The development of new imaging system by 3M is making good progress. Some technical problems such as system noise as well as electronic and image processing are being addressed. A prototype system is expected at Georgetown this spring.

4.3 Telemammography and compatibility with MDIS

We will continue working with Loral Corporation, MDIS contractor, MDIS program office, and Dr. Smith and Dr. Letkie of US Army, and NASA to study MDIS compatibility and telemammography.